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Radiological evidence of subclinical dysphagia in motor neuron disease

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Abstract Dysphagia in motor neuron disease (MND) may lead to dangerous complications such as cachexia and aspiration pneumonia. Functional evaluation of the oropharyngeal tract is crucial for identifying specific swallowing dysfunctions and planning appropriate rehabilitation. As part of a multidisciplinary study on the treatment of dysphagia in patients with neuromuscular diseases, 23 MND patients with different degrees of dysphagia underwent videoflouroscopy, videopharyngolaryngoscopy and pharyngo-oesophageal manometry. The results of the three instrumental investigations were analysed in order (1) to define the pattern of swallowing in MND patients complaining of dysphagia; (2) to evaluate whether subclinical abnormalities may be detected; and (3) to assess the role of videofluoroscopy, videopharyngolaryngoscopy and manometry in the evaluation of MND patients with deglutition problems. Correlations between the instrumental findings and clinical features (age of the patients, duration and severity of the disease, presence and degree of dysphagia) were also assessed. The results of our study showed that: (1) The oral phase of deglutition was compromised most often, followed by the pharyngeal phase. (2) In all patients without clinical evidence of dysphagia, subclinical videofluoroscopic alterations were present in a pattern similar to that found in the dysphagic group. (3) Videofluoroscopy was the most sensitive technique in identifying oropharyngeal alterations of swallowing. Impairment of the oral phase, abnormal pharyngo-oesophageal motility and incomplete relaxation of the upper oesophageal sphincter were the changes most sensitive in detecting dysphagia. Videofluoroscopy was also capable of detecting preclinical abnormalities in non-dysphagic patients who later developed dysphagia. Practical guidelines for the use of instrumental investigations in the assessment and management of dysphagia in MND patients are proposed.

Key words Motor neuron disease (MND) · Deglutition disorders · Videofluoroscopy · Videopharyngolaryngoscopy · Manometry

Introduction

The degeneration of bulbar motor neurons in motor neuron disease (MND) leads to dysphagia, dysarthria, atrophy and fasciculations of the tongue. Bulbar involvement generally occurs late in the course of the disease, but in about one-third of the cases it is present at the onset [7]. The oral and pharyngeal phases of deglutition are the most compromised as a consequence of the impairment of the lower cranial nerves, whose motor nuclei degenerate in MND [9].

Patients who develop dysphagia are at major risk for severe weight loss and aspiration and need supplemental

feeding through a percutaneous endoscopic gastrostomy (PEG) [13, 29] or nasogastric tube. Oropharyngeal rehabilitation might be useful in delaying the need for enteral feeding and in improving the quality of life of patients with neurogenic dysphagia [11, 27].

To provide appropriate assessment and treatment for patients with dysphagia owing to neuromuscular diseases, we recently established a multidisciplinary group in Padua, which includes neurologists, otolaryngologists, oropharyngeal therapists, surgeons, radiologists and nutritionists. Besides a detailed dietary history and a coordinated clinical evaluation, instrumental investigations are often required to better define the swallowing alterations [16, 36]. This is particularly important for oropharyngeal rehabilitation programmes, since the precise localization of the swallowing abnormalities is crucial for choosing specific rehabilitative manoeuvres and postures [19, 31, 35]. According to the initial protocol of our group, MND patients suitable for oropharyngeal rehabilitation underwent a videofluoroscopic and videopharyngolaryngoscopic study of swallowing, as well as pharyngo-oesophageal manometry. Radiological alterations of swallowing in MND patients have been previously reported. One study, however, was performed with techniques less sensitive than those available nowadays [2], whereas the more recent studies have mainly focused on presurgical evaluation of patients undergoing cricopharyngeal myotomy [15, 37]. Here, we report the results of the videofluoroscopic, videopharyngolaryngoscopic and manometric studies in 23 MND patients with different degrees of dysphagia followed in our centre. The availability of data from a group of MND patients free of dysphagic symptoms allowed us to compare the pattern of their swallowing impairment with that observed in dysphagic patients and to verify whether subclinical abnormalities might be detected. We also compared the sensitivity of the three different techniques in detecting swallowing alterations and propose practical guidelines for the use of the instrumental investigations in the management of dysphagic MND patients.

Patients and methods

Twenty-three consecutive MND patients referred to our neurological centre over an 18 month period were evaluated. Only patients fulfilling the following diagnostic criteria were considered: history of progressive muscle weakness, atrophy and fasciculations, absence of objective sensory involvement, absence of sphincter dysfunction, electromyographic evidence of denervation in either at least three spinal regions or in two spinal regions plus the bulbar region.

The following features were evaluated for each patient: age at the time of the study, time since onset of the disease, extent of neurological involvement, presence and degree of dysphagia. The patients were classified in clinical subtypes, as previously described [33]: amyotrophic lateral sclerosis (ALS; lower motor neuron signs and unequivocal upper motor neuron signs) ALS with probable upper motor neuron signs (ALS-PUMNS), progressive bulbar palsy (PBP; dysphagia and dysarthria are the dominant symptoms, but concomitant upper motor neuron signs may be present), progressive spinal muscular atrophy (PSMA; only lower motor neuron signs).

All of the patients were evaluated independently by two neurologists and classified as having mild, moderate, or severe neurological involvement. The evaluation was based on the presence and severity of different objective neurological signs: muscle strength (Medical Research Council scale [22]), bulk and fasciculations, deep tendon reflexes and involvement of cranial nerves. An oropharyngeal therapist examined patients' oral, pharyngeal and laryngeal functions (motor and sensory assessment, gag reflex) and ability in controlling postural changes and respiratory functions.

The severity of dysphagia was rated according to the functional ALS Severity Scale (ALSSS) of Hillel et al. [8] and classified as: absent (normal swallowing or only nominal abnormalities, nominal abnormalities being defined as when only the patient notices slight indications of dysphagia such as food lodging in the recesses of the mouth or sticking in the throat; score 10–9 on the ALSSS), mild (minor swallowing difficulties, which allow an essentially regular diet; isolated choking episodes, prolonged mealtime and need of smaller bite size may be present; score 8–7); moderate (diet limited primarily to soft foods and need for some special meal preparation; score 6) and severe (liquefied diet, but oral intake still adequate; score 5). Patients who already needed enteral feeding when first examined (score 4–1 of the same scale) were excluded. All of the diagnostic procedures described below (videofluoroscopy, videopharyngolaryngoscopy and oesophageal manometry) were performed with the patients' informed consent. The results of all three instrumental investigations were evaluated in blinded fashion.

All of the patients were followed up at 2-month intervals. At each follow-up, the patients underwent a clinical reevaluation by a neurologist, an oropharyngeal therapist and a dietitian. No instrumental investigations were performed, apart from assessment of the respiratory function, which we routinely perform at 2-month intervals in all MND patients followed in our centre (data not shown).

Videofluoroscopy

Videofluoroscopy [or modified barium swallow (MBS)] [6, 17] was carried out during swallowing of fluid and semisolid contrast medium (barium mixture of Prontobario HD, Bracco S.p.a., Milan, Italy). A water-soluble contrast (Gastrografin, Schering S.p.a., Milan, Italy) was given when the risk of aspiration was suspected. The patient was seated upright and observed with a four-view projection (anterior-posterior, lateral, and oblique right and left). The bolus size was not calibrated, but chosen by the patient in order to optimize the performance and to resemble normal feeding as much as possible. The following were assessed: oral stasis; loss of barium in the mouth vestibula during swallowing; repetitive tongue movements; incomplete or inadequate velopharyngeal closure; vallecular, piriform or hypopharyngeal stasis; incomplete epiglottic inversion; presence of aspiration; functionality of upper oesophageal sphincter (UOS) and lower oesophageal sphincter (LOS); pharyngo-oesophageal motility. The fluoroscopic studies were recorded on videotape Sony U-Matic VO 5800 PS using Sony XBR cassettes (Sony Corporation, Tokyo, Japan).

Videopharyngolaryngoscopy

Videopharyngolaryngoscopy [1] was performed using a fibrescope (BF-P10; Olympus Optical Corp. Europe) connected to a video camera (telecam pal; Karl Storz Endoscopia, Italy). The video images were displayed on videotape Sony U-Matic (Sony VO 9600). Briefly, the patients were seated in a chair with head support. The endoscope was inserted through an anaesthetized nostril to view the nasopharynx and then advanced to achieve a panoramic view of the base of tongue, larynx, piriform sinuses and posterior pharyngeal wall. The following were evaluated: presence or absence of pooled saliva in the vallecula, piriform sinuses, base of tongue; clinging to the pharyngeal walls. The endoscope was next advanced to the vocal cords to inspect vocal fold motility, control and closure. The pres-

Table 1 Clinical features of 23 motor neuron disease patients (*M* male, *F* female, *ALS* amyotrophic lateral sclerosis, *PBP* progressive bulbar palsy, *PSMA* progressive spinal muscular atrophy, *MND* motor neuron disease)

		Dysphagic	Non-dysphagic
No. of cases	Total	16	7
	M	6	4
	F	10	3
Mean age (years) (SD)	Total	64.5 (4.9)	51.6 (11.0)
	M	65.6 (4.6)	44.8 (8.3)
	F	63.8 (5.2)	60.6 (6.7)
Mean duration of symptoms (months) (SD)	Total	25.6 (26.7)	10.9 (4.4)
	M	28.5 (34.7)	11.3 (5.7)
	F	23.9 (22.5)	10.3 (2.9)
Clinical subtypes (no. of cases)	ALS	5	5
	PBP	7	0
	PSMA	4	2
Severity of MND (no. of cases)	Mild	5	3
	Moderate	4	2
	Severe	7	2

ence of appropriate sensation was evaluated by touching sequentially various areas of the laryngopharynx with the tip of the fibrescope. Deglutition tests were performed with the endoscope positioned to achieve a panoramic view of the laryngopharynx, while the patient was given small amounts of yogurt and water coloured with methylene blue. The efficacy of swallowing was evaluated based on the amount and location of residual food after swallowing. The occurrence of aspiration was inferred by observing food spill into the airway or in the epiglottis.

Pharyngo-oesophageal manometry

Pharyngo-oesophageal manometry was performed with a low-compliance infused system following the methodology already described [28]. Briefly, a multilumen catheter was used: four side-holes were located at the same level and oriented at 90° and four other side-holes were spaced at intervals of 5 cm. Data were acquired at 20 and 50 Hz, and stored in a computer for further analysis. The test was performed after an overnight fast. The catheter was passed through an anaesthetized nostril into the stomach, and the gastric pressure was assumed as the baseline. The catheter was then withdrawn through the cardia by a puller device at a slow constant speed (1 mm/s), while the subject breathed normally. We evaluated the resting pressure of the LOS, the overall and abdominal length. The catheter was then positioned with the four radial side-holes located inside the LOS, with the others 5, 10, 15 and 20 cm above, along the entire length of the gullet. The motor function of the oesophageal body and the LOS relaxation at swallowing were assessed by 10 wet swallows (5 ml of water) at intervals of 30 s. The amplitude, duration and peristaltic characteristics of oesophageal contractions (peristaltic, simultaneous or non-propagated) were considered. The motor function of the UOS and the pharynx was then assessed positioning the four radial side-holes at the level of the UOS, having two other side-holes in the pharynx, 5 and 10 cm above the UOS. Function at swallowing was evaluated with 5 wet swallows (10 ml of water), considering the amplitude, duration and coordination of pharyngeal contractions and the percentage of UOS relaxation compared with the basal resting pressure. Data from 15 healthy subjects (mean age 34 years) were obtained for comparison, using the same technique and instrumentation.

Statistical analysis

Given the non-normal distribution of the data, non-parametric tests were used. The Spearman, the Mann-Whitney and the Fisher exact test were used when appropriate.

Results

Clinical features of the patients

Twenty-three MND patients, 10 male and 13 female, were included in our study. Their clinical features are summarized in Table 1. Sixteen of the 23 patients complained of dysphagia at the time of the study: according to the ALSS, 6 (3 PSMA, 2PBP, 1 ALS) had mild dysphagia, 9 (4 PBP, 4 ALS, 1 PSMA) showed moderate dysphagia and 1 (PBP) exhibited a severe degree of dysphagia. The 7 patients with absent dysphagia, or only nominal swallowing abnormalities, were classified as non-dysphagic.

Non-dysphagic patients had a significantly lower age at onset, mainly owing to a younger male population ($P<0.05$, Mann-Whitney test). Of all the features analysed, the presence of dysphagia correlated significantly only with age, increasing over 60 years ($P<0.05$, Fisher exact test).

In our clinical follow-up, all non-dysphagic MND patients developed dysphagia after a mean period of 7.4 months (range 4–27 months, SD 7.3) from our first clinical evaluation.

Videofluoroscopy

Videofluoroscopy was performed in 20 patients, 13 with dysphagia (4 mild and 9 moderate) and 7 without dysphagia. The videofluoroscopic findings are shown in Table 2. Radiological alterations were found in 12 out of 13 with clinical dysphagia. As expected, the number and severity of alterations was higher in the group of patients with moderate dysphagia compared with the group with mild dysphagia. All of the non-dysphagic patients also showed radiological swallowing abnormalities.

We tried to identify the alterations that were more sensitive in disclosing dysphagia. These were: impairment of the oral phase, abnormal pharyngo-oesophageal motility and incomplete relaxation of UOS (Fisher exact test). The same features were the most sensitive in revealing subclinical dysphagia. In fact, we found a trend of an inverse correlation (Spearman's $\rho=-0.50$) between the number of these alternations in patients without dysphagia at the time of the study and early presentation of dysphagia in the fol-

Table 2 Videofluoroscopic findings in 20 MND patients (*s* significant, *ns* not significant, *UOS* upper oesophageal sphincter, *LOS* lower oesophageal sphincter)

Alterations[a]	Dysphagic (13 patients)	Non-dysphagic (7 patients)	P<0.05
Oral stasis of residual barium	9	3	ns
Piecemeal swallow	6	0	s
Vallecular, piriform or hypopharyngeal stasis	4	2	ns
Deviant epiglottic function	4	1	ns
Aspiration	6	0	s
Incomplete relaxation of UOS	7	6	ns
Decreased pharyngo-oesophageal motility	8	4	ns
Incomplete relaxation or hypotonia of LOS	3	1	ns
Normal	1	0	ns

[a] More than one alteration may be present in the same patient

Table 3 Videopharyngolaryngoscopic findings in 22 MND patients

Alterations[a]	Dysphagic (15 patients)	Non-dysphagic (7 patients)	*P*<0.05
Reduced velar elevation	5	1	ns
Laryngeal hypomobility	4	0	ns
Stasis in piriform sinuses	4	0	ns
Abnormal swallow test			
with thick liquid (yogurt)	4	0	ns
with thin liquid (water)	3	0	ns
Aspiration	3	0	ns
Normal	7	6	ns

[a] More than one alteration may be present in the same patient

Table 4 Manometric findings in 20 MND patients

Alterations[a]	Dysphagic (15 patients)	Non-dysphagic (5 patients)	*P*<0.05
Hypotonia of the proximal pharynx	7	3	ns
Incomplete UOS opening	4	4	ns
Alterations in oesophageal body motility	1	0	ns
Incomplete LOS[b] opening	6[b]	2	ns
Normal	3	1	ns

[a] More than one alteration may be present in the same patient
[b] Increased LOS resting pressure was also present

low-up period. The lack of statistical significance is probably owing to the small number in our sample.

Videopharyngolaryngoscopy

Twenty-two patients underwent videopharyngolaryngoscopy. This examination was not sensitive in detecting swallowing alterations either in dysphagic or in non-dysphagic patients. In fact, it showed a normal pattern in 7/15 dysphagic and in 6/7 non-dysphagic patients. The most common alterations are summarised in Table 3.

Pharyngo-oesophageal manometry

Pharyngo-oesophageal manometry was performed in 20 patients. The evaluated patients showed LOS pressure and length similar to controls, as well as amplitude and duration of contractions at any oesophageal level. However, as a group, when compared with controls, they showed a significant reduction both in the number of complete LOS relaxations and in the percentage relaxation compared with the resting LOS pressure ($P<0.05$, Fisher exact test). They also showed a reduction in the peristaltic propagation of oesophageal contractions and a higher percentage of synchronous and non-transmitted contraction sequences ($P<0.05$, Mann-Whitney test).

In the pharyngo-oesophageal segment, UOS pressure and length and amplitude of pharyngeal contractions were again similar to those of healthy controls, but MND patients had a reduced number of complete UOS relaxations and decreased percentage relaxation compared with UOS resting tone. Further, they often showed a “shoulder” before the pharyngeal contraction, indicating a reduced compliance of the oesophagus at this level [3]. Table 4 lists the abnormal manometric findings observed. The alterations more sensitive in revealing dysphagia were abnormal UOS opening and hypotonia of the proximal pharynx (Fisher exact test). The manometric test was normal in four patients (three dysphagic and one non-dysphagic).

Discussion

The results of our study showed that in MND patients the oral phase of swallowing is the most compromised, followed by the pharyngeal phase.

The oral phase is electively studied by videofluoroscopy, while the pharyngeal phase can be evaluated also by videopharyngolaryngoscopy and, although with technical limitations, by manometry. When comparing the videofluoroscopic with the videopharyngolaryngoscopic findings in the 19 patients who underwent both examinations, videofluoroscopy showed a significantly greater sensitivity ($P<0.05$, chi-square test) in detecting swallowing alterations, expecially when silent. Impairment of the oral phase, abnormal pharyngo-oesophageal motility and in-

complete relaxation of the UOS were the videofluoroscopic changes most sensitive in disclosing dysphagia. This pattern of alterations was not found in patients with oropharyngeal dysphagia owing to other neuromuscular diseases [4]. The presence of aspiration was detected by videofluoroscopy in 6 dysphagic patients, in 3 of whom aspiration was clinically silent, while videopharyngolaryngoscopy evidenced signs of aspiration in only 3 cases, all with clinically evident aspiration.

A further advantage of videofluoroscopy is that it identifies exactly when aspiration occurs (i.e. before, during or after the pharyngeal phase), giving crucial information for appropriate programmes of oropharyngeal rehabilitation [18]. Moreover, even in the absence of radiological evidence of aspiration, some videofluoroscopic alterations may be predictive of aspiration [30].

Manometric findings need to be interpreted with caution. Although as a group the MND patients had a higher number of incomplete UOS openings than controls and also a significantly increased "intra-bolus" pressure of the pharynx, dysphagia was only related to the presence of a defective oropharyngeal phase of swallowing, as shown by videofluoroscopy. Incomplete UOS opening at swallowing was equally present both in dysphagic and non-dysphagic patients, but only one patient with dysphagia had an altered UOS function with no defective oral phase of swallowing. These data confirm that the main cause of dysphagia in MND patients is a defective oral phase of swallowing and that only a minority of patients show UOS dysfunction and could benefit from cricopharyngeal myotomy [21]. This may explain the contrasting results after cricopharyngeal myotomy in these patients, as reported in the literature [5, 14, 15, 20, 23–25, 37].

We found a correlation between the age at the moment of the study and the risk of developing dysphagia. Nonspecific alterations of the oropharyngeal phase of swallowing have been described with aging in the normal population [34], but they do not seem to significantly impair the dynamics of swallowing [10]. We cannot exclude, however, that they may contribute to dysphagia in our MND population.

An interesting observation of the present study is the videofluoroscopic finding of asymptomatic swallowing alterations in all non-dysphagic MND patients. Abnormal radiological findings in MND patients without clinical evidence of dysphagia have been previously reported [15, 32]. It should, however, be noted that the possibility of false positives cannot be formally excluded, given the absence (for obvious ethical reasons) of an age-matched control group of normal subjects. However, the most common pattern of changes observed in our non-dysphagic population is similar to that found in the dysphagic group, suggesting that these changes might be subclinical or preclinical swallowing alterations. The results of the ongoing follow-up study of our MND population seem to support this hypothesis. The small number of non-dysphagic patients, however, does not permit a general conclusion to be reached. Furthermore, the interpretation of these data may be biased by the fact that all our patients without dysphagia at the initial evaluation eventually developed degluition problems. Although swallowing difficulties are common in MND, not all patients necessarily develop dysphagia, but our limited series did not include any of the latter cases.

Finally, our data (Tables 2 and 3) confirm the role of videofluoroscopy as a powerful technique in the assessment of oropharyngeal functionality, significantly more sensitive than videopharyngolaryngoscopy in revealing deglutition abnormalities.

Based on our experience with the multidisciplinary approach to MND dysphagic patients, we developed the following practical guidelines:

A. If a programme of oropharyngeal rehabilitation is planned, we always perform a preliminary videofluoroscopic study of swallowing, and an individualized treatment is carefully designed on the basis of the radiological findings and of the clinical evaluation [11, 27].

B. If videofluoroscopy is not available, or if the patient cannot be positioned for the study or is bedridden, we recommend at least a videopharyngolaryngoscopic study of swallowing. Although less sensitive than videofluoroscopy, videopharyngolaryngoscopy is accurate in excluding other organic causes of dysphagia and can also indirectly detect the presence of aspiration more reliably than an isolated clinical evaluation [12, 26].

C. From our personal experience on a limited number of patients, we do not suggest the use of videofluoroscopy in MND patients who still do not complain of dysphagia. The finding of subclinical swallowing alterations in non-dysphagic MND patients is at the moment of no practical use, since no preventive therapies are available. Moreover, knowledge of these alterations (the significance of which is still not clear) may have a negative psychological effect on already compromised patients, increasing the concern of patients and families about a complication that, although probable, might also not accur, or occur at a very late stage of the disease.

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